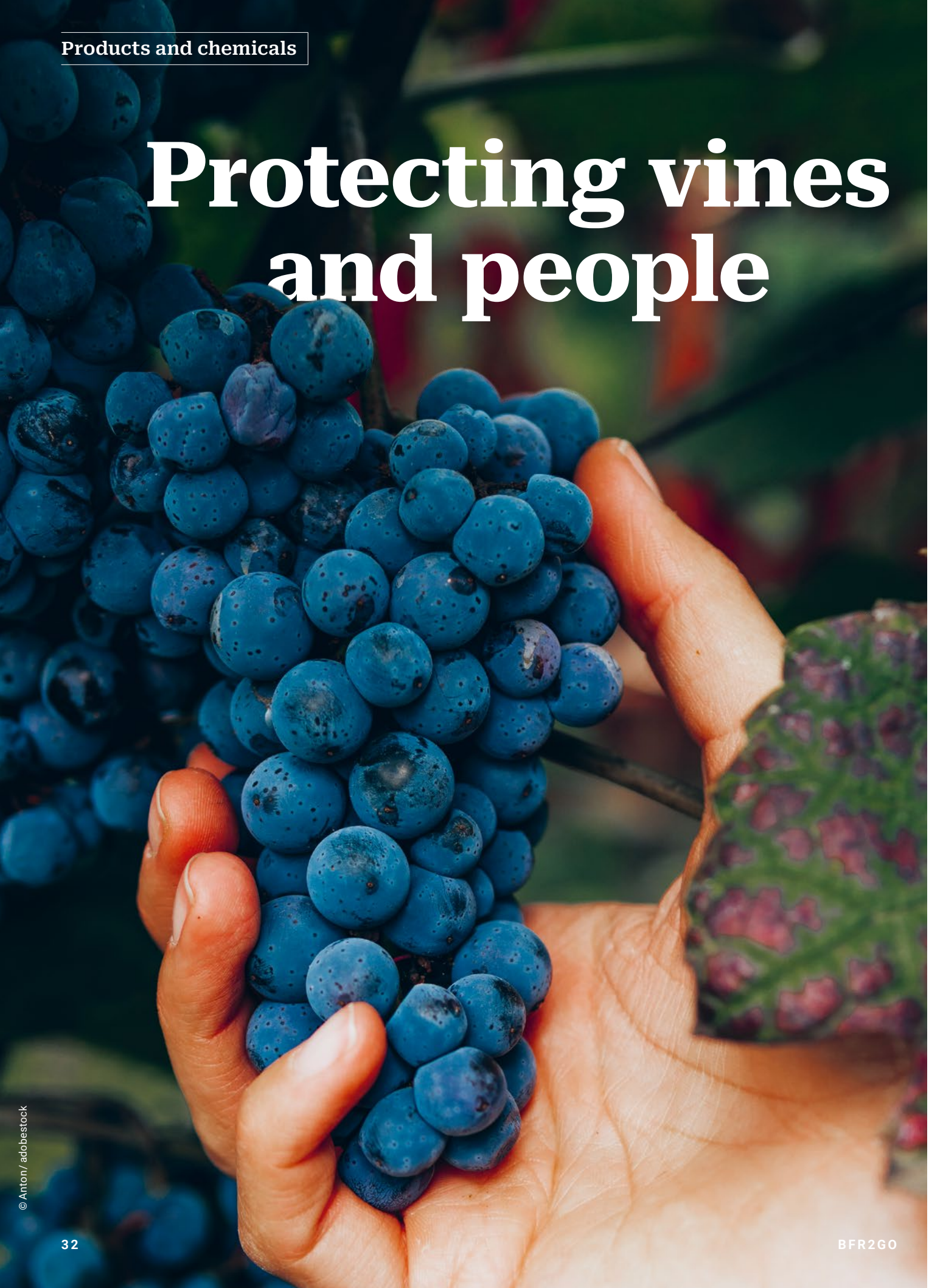
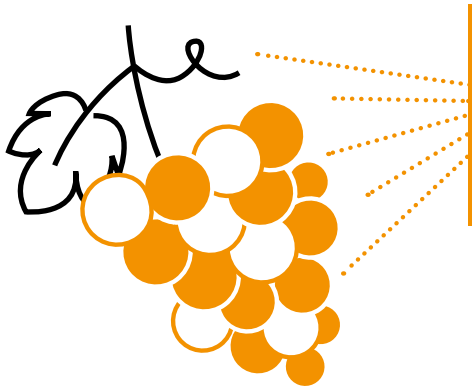
Protecting vines and people





Using vineyards as an example: What happens before a plant protection product (PPP) enters the market?

May we present: *Uncinula necator*, also known as powdery mildew. The fungus, which was unintentionally brought to Europe from North America in the mid-19th century, infests grapevines, weakens the plants, and destroys and rots the grapes. Uncinula necator is far from the only pest that affects vineyards. In order to prevent drastic reductions in crop yields, winemakers use PPP. In all likelihood, they have been doing so since antiquity. Sweet grapes have always required hard work.

Unlike in ancient times, however, PPP today are strictly assessed before they are used in fields or vineyards. The main focus is on the efficacy against the pest organism, the ecotoxicology, and the health risk assessment in terms of humans. The latter is the task of the German Federal Institute for Risk Assessment (BfR) in Berlin. Only when this comprehensive evaluation has been successfully completed, regulators give the green light for an active substance or a plant protection product.

It all starts with the regulators' approval of an active substance. This active substance is usually precisely chemically defined and is the "active" substance which will later have the decisive impact – such as on a fungus – in the PPP. The approval of an active substance is carried out at the EU level and is thus valid across the EU. It is typically limited to seven, ten or 15 years and must therefore be regularly renewed. The responsible reviewer is in each case a rapporteur Member State of the EU; for extensive evaluations there are several rapporteur Member States.

DETAILED DOSSIER

First, the applicant submits a comprehensive dossier for evaluation. The document must contain all necessary information on the active substance. Detailed data on the effects of the active substance on the organism are included in the health risk assessment. How does it enter the body and how is it metabolised and excreted? What effects can be observed? What limits and thresholds need to be adhered to in order to exclude these effects so as not to expect risks to humans? Additionally, the metabolism in the plant, potential environmental effects, and the biodegradability of the active substances in the soil are examined.

As of yet, establishing these "guardrails" for active substances has required animal experiments from which conclusions regarding humans are extrapolated. Evidence suggesting mutagenic or carcinogenic effects or negative impacts on fertility or foetal development (reproductive toxicity) for humans immediately preclude approval. The same is true for interference with hormonal (endocrine) balance.

By way of example, let us examine the tongue-twistingly termed active substance mefentrifluconazole, which is used in vineyards. The active substance blocks an enzyme which is essential for fungi such as Uncinula necator. In their comprehensive report, the scientific evaluators from the EU (the United Kingdom was the former rapporteur Member State) note the mode of action of mefentrifluconazole as well as possible mechanisms of fungal resistance and much more pertinent information. This includes practical uses, potential risks to human and animal health, residues on plants, animals and food, the retention in the environment and groundwater, and the (unintended) effect on non-target organisms.

WHAT ARE THE RISKS?

In order to gain approval, the applicant was required to present studies regarding the active substance's toxicity. Using animal experiments, short-term and long-term toxicity were assessed. Liver damage can occur with high doses of mefentrifluconazole. This is not surprising, as the active substance is metabolised in the liver as the "target organ" and then excreted into the intestine via the bile. Mefentrifluconazole's genotoxicity, carcinogenicity, reproductive toxicity,

and potential negative effects on the nervous system were also assessed. There was no meaningful evidence to this effect.

Based on the toxicity evaluations, the scientific evaluators also determine ("derive") thresholds. These values serve as orientations for daily life and human safety (including in the production process) and are set to have a large "safety margin" in relation to an actually toxic amount of an active substance. After all, it is the dose that makes the poison.

ON THIS SIDE OF THE THRESHOLD

One of the thresholds is the acceptable daily intake (ADI). This value denotes the amount of an active substance a person can consume daily for an entire lifetime without expecting adverse effects. In the case of mefentrifluconazole, the ADI according to the current evidence is 0.035 milligrams per kilogram of body weight per day. This means that a person weighing 70 kilograms could consume up to 2.45 milligrams of the active substance without exceeding the ADI and therefore without risk to health.

"Residues of plant protection products in food, such as in grapes, are possible and are taken into account in the approval process," says BfR PPP expert Dr Jens Schubert. "But the deciding factor is not if, but rather how much. Has the ADI or another threshold been exceeded?" This can, for example, lead to a product no longer being marketable and being pulled from the shelves. Once the rapporteur Member State has received the draft assessment report for the active substance, it is published for comments. After a final consultation, the European Food Safety Authority (EFSA) prepares the final version of the report, the EFSA conclusion. The final vote on the approval is then taken by a committee of the European Commission. The scientific assessment, including comments, is then followed by the regulatory decision.

PLANT PROTECTION: TRIZONE EU

Can the active substance approved by the EU now be used in the vineyard? The answer is no, because the corresponding PPP must first be authorised. In the case of mefentrifluconazole, the product is an agent having mefentrifluconazole as the active substance as well as additives which facilitate application. The authorisation of a PPP is similar to the approval of an active substance, but there are also a few differences. For example, the assessment and the authorisation is not EU-wide, but instead regionally decided in the northern, central, and southern "zones" of the EU.

One rapporteur Member State is responsible for the assessment in a given "zone". In the case of mefentrifluconazole, that state was Austria in the central zone. The focus is on the practical application of the product. The Member State responsible evaluates, for example, what pests the active substance is effective against, where it may be used, what dose is required, and what ecological consequences are likely to be expected. In Germany, PPP are authorised by the German Federal Office of Consumer Protection and Food Safety (BVL). The BVL also determines regulations for use, which include the necessary protective gear or waiting periods before harvest.

"Residues of plant protection products in food are possible and are taken into account in the approval process."

Dr Jens Schubert, BfR PPP expert

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FIGHTING FUNGI WITH COPPER AND SULPHUR

Organic farming does without artificially produced active substances. This means that mefentrifluconazole is off-limits. Instead, use is made of products with a plant or microbial basis or of naturally occurring chemical compounds. In the case of fungi on grapevines, the most commonly used solutions contain copper salts or sulphur. Copper and sulphur compounds have been used in agriculture for more than 200 years. These active substances also have undesirable toxicological effects on humans above a certain dose and must, just like "synthetic" products, be regularly approved and the corresponding PPP must subsequently be authorised. One example of such a product in organic winemaking contains copper sulphate, whose copper ions penetrate the fungal spores and then target proteins and enzymes. The second active component is elemental sulphur, which, inter alia, acts by breaking down the cell membranes of fungi to dry them out. The product works on both powdery and downy mildew. A drawback of copper, however, is that it accumulates in the soil. It turns out that "natural" solutions also have their pros and cons.—

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"Natural" solutions also have pros and cons.

More information

BfR information
"Plant protection products"

Approval of PPP active substances
(EU-wide)

1. Application by applicant including further data and studies on the active substance

2. Draft of an assessment report by a rapporteur Member State
including further data from third parties (in Germany in collaboration with the BfR)

commenting phase by Member States, applicants, the public

answering open questions during meetings between experts from Member States

3. Conclusion by the EFSA based on the assessment report by the rapporteur Member State

4. A decision in favour of or against an active substance by the relevant committee of the European Commission.

Approval process (in the respective EU zone) (after active substance approval)